

III. REMARKS

Claim Status

Claims 1-2 and 5-13 are under current examination.

Claims 1-2 and 10-13 stand rejected; claims 5-9 stand objected to.

Claim Objections

Claims 5-8 are objected to because the claims contain the word, "SEQ ID" which the examiner suggests should be rewritten as "SEQ ID NO:"

This informality has been corrected in the amended claims.

Claim Rejections - 35 USC § 112

Claims 1-2, and 10-13 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because claim 1 is broadly drawn, such that it applies to any a genus of Gaq-Gustducin chimeric G-protein wherein the last 44 amino acids of the Gaq protein sequence are replaced with a 44 amino acid unit of Gustducin. However, the working examples provided in the instant application only demonstrate individual species of Gaq-Gustducin chimeric G-protein, specifically SEQ ID NO:2.

The examiner argues that although the specification has support for the claim language of the newly amended claim 1, the specification does not define which 44 amino acids of Gustducin

can be used to replace the C-terminus of the G protein.

Considering the potentially large numbers of polypeptides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Applicant has amended claim 1 to further define the identity of the 44 amino acids to conform to the requirements of 35 USC 112. The claims now specifically identify the last 44 amino acids of the Gaq sequence. These amino acids are identified as those as set forth in the SEQ ID 2. Furthermore, the Gaq-gust44 chimeric G-protein itself is identified as having a sequence homology of at least 90% to SEQ ID NO:2. basis for the 90% homology appears in the specification at page 5, fifth paragraph.

This amendment limits to the specific gustducin-derived 44 amino acids of the chimeric protein, i.e. the C-terminal amino acids of gustducin.

Applicant believes the amended claims fully meet the requirements of the statute and are therefore are in form for allowance, which is respectfully requested.

Claim Rejections - 35 USC § 103

Claims 1-2, and 10-13 are rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6

October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

The previous office action rejected Claims 1-6 and 9-17 under 35 U.S.C. 103(a) as being obvious over Margolskee (USP 5,817,759) in view of Yao et al. (USP 7,041,457).

Applicant's response to the previous office action overcame this rejection which was expressly withdrawn.

Thus, the only additional art is Ruiz-Avila et al. The examiner utilizes Ruiz et al., at pages 8, 10 and 11 of the office action, as art teaching that the interaction of Gustducin with its cognate taste receptors is similar to that of transducing with rhodopsin. Ruiz-Avila et al. is also used as art disclosing the nexus between Gustducin and transducing homology and the importance of the C-terminus for interacting with taste receptors.

In applicant's response to the last office action applicant highlighted the fact that page 4 of the specification states:

"Surprisingly we have now found that chimeric G-proteins based on Gaq-Gustducin are able to bind to a wide range of known and putative bitter taste receptors, and sweet and umami receptors with high affinity.

and that Margolskee does not disclose chimeric proteins.

Ruiz-Avila et al. is cited by the examiner as disclosing the importance of the C-terminus for interacting with taste receptors. But this is already disclosed by Yao et al. In Yao et

al.'s claim 1 the claim requires the replacement of at least 5 amino acid residues from the C-terminus of a mutated G_q protein. Yao et al. state, in their specification:

For instance, the present inventors have also discovered that the Gly to Asp mutation is synergistic with the replacement of the C-terminus of G α_q by that of transducin or G α_{olf} . G α_q proteins containing C-terminal amino acids from transducin or G α_{olf} in combination with a Gly66 to Asp alteration show increased activity compared to individual chimeras alone. A preferred embodiment is a variant G_q proteins having at least about five amino acids in the C terminus of said G_q protein replaced by at least about five amino acids from the C terminus of G α_{olf} , if or transducin, wherein said C-terminal substitution increases promiscuity of said variant G_q protein as compared to the corresponding native G_q protein. Up to 44 amino acids of the C terminus of transducin or G α_{olf} may be incorporated. Other possible variants are shown in FIGS. 3 and 4.

Thus, it appears that Ruiz-Avila et al. is merely additive to Yao et al. and that the examiner, having already acknowledged that applicants have overcome the art cited in the previous action, has not made out a new *prima facie* case.

Yao et al. is directed to chimeric proteins and discloses a G_q-transducin44 chimeric protein that is 58% homologous to the G16gust44 chimeric protein of the invention i.e. very much different from the claimed chimeric G-Proteins which are 90%

homologous to SEQ ID NO:2.

Margolskee merely discloses Gustducin, but no chimeric G-proteins. Ruiz-Avila et al. is not directed to chimeric G-proteins either, and does not disclose the suitability or interchangability of either transducin or gustducin in a chimeric G-protein.

Ruiz-Avila et al. exclusively addresses the natural interaction of gustducin and, commenting on various studies, mentions that the latter suggest that the interaction of gustducin with its cognate taste receptors, a key determinant of which is its C-terminus, may be similar to that of transducin with rhodopsin. Notably, the latter does not suggest anything in terms of actual functionality of one or the other partial protein in a chimeric protein, neither correct folding, coupling efficiency of the G-protein to the chimeric receptor nor resulting signal strength. This is significant in light of the fact that the **native** version of the claimed G-proteins (G15, G16 and their homologs) do not couple effectively, in contrast to the **chimeric** G-proteins that are claimed.

Therefore, the addition of Ruiz-Avila as a third document does not disclose information that would allow one skilled in the art to arrive at the invention - the skilled person finds no direction whatsoever on which components may be combined in which way to result in a fully functional chimeric G-protein, much less a chimeric G-Protein with an improved coupling efficiency.

An artisan would therefore not be motivated to make the

claimed chimeric G-Protein, nor would have expected success based on Yao et al.'s chimeric G-Proteins, which share only about 60% homology with the claimed chimeric Gaq-gust44-Proteins.

Applicants believe the amendments to the claims and the above explanations are sufficient to negate any *prima facie* case of obviousness and respectfully request favorable reconsideration and allowance of these claims.

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

Respectfully submitted,
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